A systematic review of the effects of dietary interventions on neonatal outcomes in adolescent pregnancy

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A systematic review of the effects of dietary interventions on neonatal outcomes in adolescent pregnancy

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Abstract

Background. Poor nutrition negatively impacts on pregnancy outcome, fetal growth and neonatal survival. Adolescent mothers, with competing demands of a growing baby and their own rising nutritional requirements, often have poor diets. Despite recognition of their physiological immaturity and nutritional inadequacies, along with evidence highlighting significant differences between adolescent and adult pregnancy outcomes, systematic evidence on the effects of supplementation on adolescent pregnancy is scarce.

Aim. To evaluate the effectiveness of dietary interventions on neonatal outcomes in adolescent pregnancy (19 and under).

Method. CENTRAL, EMBASE, CINAHL, Cochrane, Maternity and Infant Care, Scopus and MEDLINE databases were searched using selected terminology. Titles and abstracts were screened with selected papers reviewed in full by two authors against the inclusion criteria. Any randomised controlled trials in which the effects of nutritional interventions were evaluated in adolescent pregnancy were included. Data were extracted on study quality, design, compliance, dose and duration of intervention, and main birth outcomes, and analysed using Review Manager.

Results. Five studies out of 18 identified were included. Four used supplementation (three zinc, one calcium) with one intervention comparing dairy products to fortified orange juice. The limited available data showed a significant effect from zinc supplementation in reducing the likelihood of low birthweight (RR [95%CI]: 0.39 [0.15, 0.98], one study, n=507) and that having four servings of dairy per day increased average birthweight in adolescent pregnancy (MD [95%CI]: 240g [110.83, 369.17]).

Conclusion. High-quality comparative studies between supplements and food sources to improve birth outcomes for adolescent pregnancies, focusing on the clinical effectiveness and acceptability are urgently needed.

Keywords: Adolescent, micronutrient, pregnancy, interventions, randomised controlled trials, evidence-based midwifery

Introduction

Nutrition is an important modifiable factor affecting pregnancy outcome, fetal growth and neonatal survival (Redmer et al, 2004; Lechtig et al, 1975). Infants, who are growth-restricted due to poor intrauterine nutrition, may potentially be programmed to develop cardiovascular disease, diabetes and obesity later in life (Godfrey and Barker, 2000; Barker, 1998).

Poor nutrition is of a greater concern for adolescent mothers who are faced with the demands of a growing baby in addition to their own rising nutritional requirements. The concept of competing growth needs of adolescent mothers with that of their fetuses was first proposed by Naeye (1981) and further strengthened by other investigators demonstrating smaller birthweight in adolescent compared to adult pregnancies (Scholl et al, 1994; Frisancho et al, 1983). In addition, several studies have shown an association between nutritional deficiencies and low birthweight (Baker et al, 2009), pre-term birth (Ramakrishnan et al, 2012), morbidity and mortality for babies born to adolescents (Gilbert et al, 2004). This is further complicated as adolescent mothers are predominantly from socio-economically deprived backgrounds linked to poor diets and smoking (Conrad, 2012).

Micro- and macronutrients have essential roles in optimising fetal growth and pregnancy outcome; however the focus of this review will be on micronutrients. Due to more efficient utilisation and absorption of nutrients, no increase in dietary intake during pregnancy is necessary (Williamson, 2006). However, partly based on survey evidence suggesting poor dietary intake, an increase in several micronutrients, including folate, vitamins B1, B2, C, A and D, is recommended (Williamson, 2006). A UK national survey of adults (19 to 64 years) indicated many women of childbearing age did not meet their nutrient requirements, which have considerable implications for pregnancy outcome (Henderson et al, 2003). Their data also suggests an adverse relation between age and proportion of women with intake from all sources (food and supplements) below the lower reference nutrient intake (LRNI). Poor nutritional intakes and hectic dietary patterns in adolescents have been illustrated by several investigators (Baker et al, 2009; Burchett and Seeley, 2003). Additional maternal calcium intake for adolescent pregnancies has been advised due to rapid growth and bone development in adolescents competing with the needs of the growing fetus (Williamson, 2006).

Despite a common appreciation of the physiological immaturity in adolescent pregnant mothers and their nutritional inadequacies, along with evidence suggesting significant differences between adolescent and adult pregnancies regarding fetal and neonatal wellbeing, systematic evidence on the effects of nutritional supplementation on their pregnancy outcome is scarce. The existing reviews mainly focus on adult pregnancies and the effects of single or multi micronutrients. They also include a wide age range without specifically reporting the results for teenage pregnant women (Hofmeyr et al, 2014; Ramakrishnan et al, 1999). Given the importance of vitamins and minerals in supporting a healthy pregnancy outcome, and the evidence on nutritional deficits, a systematic evaluation of the impact of nutritional interventions on pregnancy and birth outcomes is needed to inform interventions aimed at reducing health inequalities for these vulnerable women and their babies.

Aim

The aim was to evaluate the effectiveness of nutritional interventions on neonatal outcomes for adolescent mothers, assessed through randomised controlled trials (RCTs). For the purpose of this review, nutritional interventions included both dietary interventions and nutritional supplementation.

Method

Search strategy

The authors searched the following databases, from inception to 2 February 2015, for relevant studies: CENTRAL (via Cochane Library), CINAHL Plus with Fulltext (via EBSCOHost), Embase (via NICE Evidence), Maternity and Infant Care (via Ovid), MEDLINE (via EBSCOHost) and Scopus. The search strategy had four main strands – pregnancy, adolescents, dietary interventions and RCTs – designed to capture all papers published regarding diet-based interventions during teenage pregnancy. The authors used text words and relevant indexing to capture the concept of nutritional interventions and teenagers and pregnancy. Additionally, the Cochrane Highly Sensitive Search Strategy for identifying RCTs in MEDLINE, sensitivity- and precision-maximising version revision was adapted to limit the search results to RCTs (Higgins and Green, 2011). The reference lists of included papers were assessed for additional relevant studies, which generated one new paper (Cherry et al, 1989). No language restriction was applied.

Inclusion criteria

The authors considered all RCTs in which the effects of nutritional interventions, including vitamin and mineral supplementations (individually or combined) and dietary supplementations, such as foods rich in nutrients, were evaluated in adolescent pregnant women.

Outcome measures

- Low birthweight (birthweight less 2500g)
- Pre-term birth (gestational age less than 37 weeks)
- Birthweight
- Perinatal mortality (fetal death ≥24 gestational weeks and neonatal deaths in the first week of life).

Data extraction and quality appraisal

Two review authors independently assessed the suitability of identified papers, according to the inclusion criteria. Any disagreement was resolved by consulting a third author. One reviewer extracted data using a specific data extraction form and entered the data into the Review Manager software (Nordic Cochrane Centre and The Cochrane Collaboration, 2012), which was subsequently double-checked by a second reviewer. Clarification was sought from all authors of included studies where there was ambiguity, with no success in receiving additional required information. All the studies were assessed for the risk of bias (Higgins and Green, 2011) and were categorised as high, low or unclear risk of bias in sequence generation (for example, low risk if computerised central randomisation was reported), allocation concealment (for example, low risk if opaque sealed envelopes were used), blinding (for example, low risk if placebo was used), incomplete outcome data (for example, high risk if attrition rate was higher than 20%), selective reporting bias and other sources of bias, such as extreme baseline imbalance or whether the trial was stopped early.

Data synthesis

The authors used the mean difference and standard deviations for presenting outcomes from continuous data and expressed summary risk ratios for dichotomous data with 95% confidence intervals (95% CI), using a random effect model due to both clinical and statistical heterogeneity. Due to variation in the type of intervention (for example, different nutrients) overall meta-analysis was not performed, however, data was pooled together at the sub-group level for each nutritional intervention. The statistical heterogeneity in each meta-analysis was assessed using the T^2 (Tau squared), I^2 and Chi^2 statistics. A substantial heterogeneity was considered if I^2 was greater than 30% and either T^2 was greater than zero, or the P-value in the Chi^2 test was less than 0.10. The data were analysed on the basis of intention-to-treat, therefore, the authors included all participants randomised to each group in the analysis.

Results

The database searches yielded 1224 records, citation and reference searching yielded three additional references, after duplicates were removed, 806 proceeded to screening based on title and abstract, of which 18 articles were deemed relevant. Out of 18 identified potential articles, 13 were excluded and five were included (Chan et al, 2006; Castillo-Durán et al, 2001; López-Jaramillo et al, 1997; Cherry et al, 1989; Hunt et al, 1985).

Excluded studies

Of the 13 studies which were excluded, six were not RCTs (Davis et al, 2013; Tange et al, 1993; Cherry et al, 1991; Dawson and McGanity, 1989; 1988; Dawson et al, 1989). The studies by Diogenes et al (2013a; 2013b; 2011) were very similar RCTs using calcium and vitamin D supplementation to improve maternal bone mass in lactating adolescent mothers, but were excluded as there was no reporting of outcome measures of interest with a lack of clarity on the quality of the study. Two were excluded due to a lack of sufficient information to allow assessing their eligibility for inclusion and attempts to contact the authors for further information were not successful (Herrera et al, 2006; Nogueira et al, 2003). Meier et al (2003) investigated the effects of iron supplementation, which was excluded due to not reporting the outcomes of interest to this review. Finally, one study (Christian et al, 2013) conducted a three-arm intervention comparing vitamin A, β-carotene and placebo groups in Bangladesh using a cluster RCT design including 7730/17,895 (43%) adolescent mothers, which did not report separate outcomes for the group of interest and the attempts of these authors in contacting Christian et al (2013) failed to provide specific information relevant to this review.

Included studies

The age of participants in the included studies were 19 years or less (see Table 1). The type, dose and duration of supplementation use varied between the five included studies (see Table 1), therefore, the results are reported separately for each type of intervention, where outcomes of interest were reported. Four included studies used supplementation. Three of these studies used zinc supplementation versus placebo (Castillo-Durán et al, 2001) in Chile and (Cherry et al, 1989; Hunt et al, 1985) in the US and one used calcium supplementation versus placebo (López-Jaramillo et al, 1997) in Ecuador. The final study used dairy products compared to orange juice fortified with calcium (those who did not tolerate the fortified orange juice, used calcium supplementation as well) compared to the control group (Chan et al, 2006). Three of the included studies reported that their participants were from a low socio-economic status, a state-supported hospital or rural areas (Castillo-Durán et al, 2001; Cherry et al, 1989; Hunt et al, 1985) and Chan (2006) recruited from the university's teen mother and child programme or private clinics. The age of participants ranged from 14 to 19 years with a mixture of primipara and multipara women.

Risk of bias in included studies

Most of the strategies used to reduce bias in the included studies were poorly described. To limit performance bias, all studies except Chan et al (2006) blinded participants and personnel, which is logistically possible with placebo versus supplements. This was not possible in Chan et al's (2006) intervention, as participants knew if they were taking a calcium supplement, calcium supplement and orange juice or dairy products. Chan et al (2006) clearly mentions random sequence generation and allocation concealment to reduce selection bias, however, the other five studies were not explicit. There was a lack of clear description for the other studies leading to those being scored as unclear. Chan et al (2006), Cherry et al (1989) and Hunt et al (1985) had very low attrition rates (<13%), but Castillo-Durán et al (2001) had a much higher attrition rate (37%), which could lead to bias.

Effects of interventions

Low birthweight

Two studies were available; one reporting the effects of zinc and the other the effects of calcium supplementation on the incidence of low birthweight in adolescent mothers. Zinc supplementation reduced the likelihood of low birthweight compared to the control group (RR [95%CI]: 0.39 [0.15, 0.98], one study, n=507). In the only study (López-Jaramillo et al, 1997) that reported this outcome for calcium supplementation, there was no incidence of low birthweight in either arms of the study to enable comparison of the results.

Pre-term birth

Three studies reported the results for this outcome; two reporting the effects of zinc and one the effects of calcium supplementation on the incidence of pre-term birth in adolescent pregnancies. The incidence of pre-term birth was not significantly different in the existing studies: zinc

Table 1. Summary of included studies showing the supplement or food dose, duration and compliance

Study	Study aims/ participants' age	Control supplements/ day	Intervention supplements/ day	Timing of intervention	Attrition rate (1%)
López-Jaramillo et al (1997)	Calcium supplementation and pre-eclampsia (Ecuador: <17.5yrs)	(n=135)	(n=125) 2000mg calcium (taken as 4 x 500mg)	20 weeks – delivery	1
Chan et al (2006)	Dietary calcium interventions (US: 15-17yrs)	(n=23)	(n=24) Orange juice + calcium taken as fourservings per day, to provide 1200mg Ca (n=25) Dairy taken as four servings per day to provide 1200mg Ca	20 weeks – delivery	0
Hunt et al (1985)	Zinc supplements for low income Mexican-descent adolescents (US: <17yrs)	(n=68) multivitamin	(n=70) multivitamin + 20mg zinc	<19 weeks – delivery	7%
Cherry et al (1989)	Associations between zinc supplementation, maternal body weight and pregnancy outcomes (US: 13.5-19.6yrs)	(n=284) multivitamin	(n=297) multivitamin + 30mg zinc	<25 weeks – delivery	13%
Castillo-Durán et al (2001)	Zinc supplements on pregnancy outcome for adolescents (Chile: <19yrs)	(n=403) 40mg iron	(n=401) 40mg iron + 20mg zinc	6 to 20 weeks – delivery	15%

supplementation study (RR [95%CI]: 0.66 [0.42, 1.05], random test, two studies, n=1063) and no pre-term birth occurred in either intervention or control group in the only calcium study that reported this outcome (López-Jaramillo et al, 1997).

Birthweight

Four studies reported this outcome; two reporting the effects of zinc supplementation and the other two focused on calcium supplementation, one of which included a three-arm study (Chan, 2006) comparing the effects of calcium supplementation with dairy food rich in calcium and control groups in adolescent pregnant women. No significant differences were observed for birthweight between the intervention group in any of the different supplementation groups: zinc supplementation studies (RR [95%CI]: 60.49 [-17.51, 138.49], random test, two studies, n=613), and calcium supplementation (RR [95%CI]: 73.81 [-16.61, 164.23], random test, two studies, n=307). However, a significantly higher average birthweight was observed in a study by Chan et al (2006) in the arm that used dairy products compared with the control group (MD [95%CI]: 240g [110.83, 369.17]).

Perinatal mortality

Of the two studies that provided information on this outcome, López-Jaramillo et al (1997) reported no incidence of perinatal death and the only study (Cherry et al, 1989) in which fetal loss outcome was reported, showed no significant differences between the zinc-supplemented group compared to the control group (RR [95%CI]: (0.57 [0.26, 1.23], one study, n=581).

Discussion

The limited available data showed a significant effect from zinc supplementation (from early pregnancy) in reducing the likelihood of low birthweight. It also showed that nutritional interventions specifically instructing young women to have four servings of dairy product per day (from 20 weeks) can increase average birthweight for this group of women.

This review was to the authors' knowledge the first to specifically focus on adolescents, who have additional nutritional requirements during pregnancy. Other reviews have looked at single supplements (Hofmeyr et al, 2014), iron and folic acid only or multi-micronutrient supplements (Shah and Ohlsson, 2009), or were literature based only (Ramakrishnan et al, 1999) but looked at adult populations in developed and developing countries. Hofmeyr's review (2014) looked at low-dose calcium supplementation <1g/d with or without co-supplements and found calcium reduced the incidence of pre-eclampsia in all nine studies, however, only two of these studies included adolescents at higher risk of pre-eclampsia, but did not report their data separately (Herrera et al, 2006; Almirante, 1998). López-Jaramillo et al (1997) found a significant effect with 2g/d calcium for adolescents, which are in line with the WHO's (2011) recommendation for 1.5-2g/d for pregnant women in areas with low dietary intakes, such as Ecuador. Many factors should be considered when administering such high doses as calcium >800mg/d decreases iron absorption and the large calcium carbonate tablets may be a barrier to compliance and expensive or heavy to transport in large scale population studies (Hofmeyr et al, 2014).

Zinc reduced incidence of low birthweight in one study. A Cochrane review (Mori et al, 2012) into zinc found a small but significant reduction in pre-term birth, but not in numbers of low birthweight babies. They analysed 20 studies, of which 16 were in low-income settings and three were in adolescents (Castillo-Durán et al, 2001; Cherry et al, 1989; Hunt et al, 1985). However, they did not report any sub-group analysis on the adolescent women. As with many minerals, the controversy around zinc supplementation is in part due to difficulties in measuring baseline zinc status and the bioavailability of zinc from supplements or food sources (Gebreselassie and Gashe, 2011). Many women with zinc deficiency are also deficient in other nutrients (Mori et al, 2012) so would benefit from improvements to their overall diet quality. The mechanism of effects for micronutrients is poorly understood, which can limit finding interpretations.

Brantsæter et al (2012) conducted a systematic literature review of the relationship between maternal dairy consumption during pregnancy, fetal growth and birthweight in six studies, one of which was on adolescents. They found that dairy consumption had a positive effect on birthweight in 4/6 studies, however, the results for birth length were mixed. Moderate dairy consumption was most effective at improving birthweight for those who had very low baseline intakes, but larger doses above the recommended two to three servings a day may lead to excessive gestational weight gain (Brantsæter et al, 2012).

Research is required to investigate the appropriate recommended intake for optimal pregnancy and birth outcomes. In line with other prospective cohort and case control studies (Brantsæter et al, 2012), this systematic review of RCTs showed dairy products can improve birthweight in this group. There is ample evidence to suggest that there is a chaotic dietary pattern among adolescent mothers (Stanner, 2004; Burchett and Seeley, 2003) and that observation by Chan et al (2006) showing adolescent mothers complied well with taking dairy products with positive outcomes, may be worth further exploration.

Strengths and limitations

As the first systematic review of RCTs evaluating the effects of nutritional interventions in adolescent pregnant mothers, this provides collective evidence to inform future research direction for this vulnerable group in society. The scarcity of data available for adolescent pregnancies, in addition to limited understanding of the mechanisms behind the nutrition and birth outcome, restricts our interpretation of the findings. However, the gaps in knowledge identified in this review can direct future research.

The lack of sufficient data prevented the authors from conducting sub-group analyses based on type of interventions (vitamin/mineral supplementation versus foods sources), duration, timing of intervention, mother's baseline nutritional status, country of origin and level of deprivation.

The possibility of interaction among vitamins and minerals in either facilitating or hindering the absorption of other nutrients may also be another confounding factor in this review. The limited understanding of the complex physiological mechanisms between various nutrients (individual or combined) and birth outcomes may impact on the findings in studies when both the control and intervention group have been given supplements. Cherry et al (1989) and Hunt et al (1985) gave all participants (control and intervention) multivitamins and Castillo-Durán et al (2001) gave all participants 40mg iron, which may have been due to the ethical considerations.

The exact mechanisms and functional pathways of micronutrient supplementation during pregnancy are not fully understood. It is speculated that the beneficial effects of micronutrient supplementation is enforced through enhanced maternal energy metabolism and anabolic processes, as well as expansion of plasma volume due to fluid retention, which can lead to improved fetal growth (Shah and Ohlsson, 2009). In addition, improved haemoglobin levels and increased absorption of iron related to vitamin C and riboflavin, as well as improving the mother's immunity, may reduce the risk of pre-term birth by diminishing the risk of infection. There is, however, a possibility of adverse interactions among the combined nutrients by enhancing or reducing absorption of one another, and the risk of overdose. There is a significant level of clinical and statistical heterogeneity in the included studies, limiting the interpretation of the review findings. More appropriately designed studies are required to detect the effects of simple nutritional interventions.

Despite the importance of nutrition in achieving an optimum birth outcome (Ramakrishnan et al, 2012; 1999), this review showed there is a significant gap in the literature focusing on adolescent pregnancies. Small sample size, insufficient reporting of exact timing of the intervention and lack of appropriate design for outcomes of interest in achieving statistical power to detect differences among the groups were major limitations in the included studies. This was particularly of importance for perinatal mortality outcome, which is a rare event and requires a much larger sample size to detect any differences between the groups.

Conclusion

The positive effect of dairy food on improving birthweight for teenage pregnancies is encouraging. However, in light of scarcity of evidence, the results should be interpreted with caution. This review highlights the lack of high-quality studies into nutritional interventions and supplement use in adolescent pregnancy. Comparative studies between supplements and food sources to improve birth outcomes for adolescent pregnant mothers, focusing on the clinical effectiveness and acceptability are urgently needed. Further investigations are required to ascertain which dietary interventions and nutrients, or combinations of nutrients, at which dose and for which duration, are most effective at reducing adverse outcomes. Well-designed studies with appropriate baseline nutritional and biochemical measurements are needed to establish whether all adolescent mothers in developed and developing countries would benefit from a supplement, or whether only those who have significant nutritional deficiencies would benefit.

Practical, acceptable and feasible nutritional interventions with specific health behaviour change approaches are required in this vulnerable group of women.

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